

1999057813

# **PHARMACY IN SPACE**

## **A SESSION ON NASA TECHNOLOGIES**

Robert C. Richmond  
ES76 Bldg 4481  
Marshall Space Flight Center  
AL 35812

*CONF. PAPER  
-IN-52*

tel: 205/544-3418  
fax: 205/544-6660  
e-mail: robert.richmond@msfc.nasa.gov

Presented to the 145th Annual Meeting of the American Pharmaceutical Association  
Monday March 23, 1998  
Miami, Florida

### **NASA IS RELEVANT TO INTERESTS OF THE AMERICAN PHARMACEUTICAL ASSOCIATION**

In 1993, Vice-president Gore was charged with creation of a correctional plan for the poor findings from an efficiency study of governmental agencies. That correctional analysis was then used to support efforts to balance the budget in ways anticipated to improve the value returned per tax payer dollar spent. The final result was a broad initiative collectively termed "reinventing the government", which included major restructuring within NASA as well, termed "reinventing NASA". This included substantial elimination of middle management and downsizing such that about 2 million government workers employed in 1992 has shrunk now to about 1.2 million government workers who are employed in ways that at least somewhat decrease bureaucratic and programmatic inefficiencies.

Today, "reinvented NASA" has an awareness of contractual commitment to the public. NASA now operates within a so-called "strategic plan" that requires awareness and response to domestic needs. This is important to this audience because it means that NASA is committed to exploring interactions that you may wish to initiate. That is, you are urged to explore with NASA on topics of educational support, collaborative research, or commercial partnerships in drug development and application, as the pertinent examples here, in ways that can include involvement of central NASA resources and missions.

The desirable outcomes from such cooperative interactions are "spin-offs" that expand the utility of the frequently restricted market of NASA R&D. That is, products used by NASA for space exploration often find NASA as their sole user, so that NASA is often faced with the need to be the sole developer and provider of these products as well. This scenario is not fundamentally desirable, and reaching out to the domestic sector increases the brain trust from which additional use for these products can be identified and pursued. In this way, multiple users can be identified in order to provide as much public good as possible for tax dollars otherwise directed away from the economic mainstream. These efforts have forged the new interactive structure of within NASA, and this is why we can provide a session entitled "Pharmacy in Space".

## **NASA INTERESTS FOR THE AMERICAN PHARMACEUTICAL ASSOCIATION**

Dispensation of drugs is central to the job description of pharmacists. NASA technologies do not contribute much to this function directly.

It is also true that by dispensing drugs the practicing pharmacist becomes the most visible professional from whom the patient as end customer can gain information on the drug that is being prescribed by the physician. There are also pharmacy subspecialties, such as oncology pharmacists in tertiary care centers, that interact as well with physicians as the end customers, where the professional awareness of drug mechanisms and development processes is more involved. Professionally motivated pharmacists thus provide their customers with information on mechanisms of drug action, context of drug development, and an awareness of drug development. This may be the most satisfying part of the job, and is a part to which NASA technologies do contribute.

Examination of the membership of the APhA also reveals detail men and others representing all levels of the pharmaceutical industry. Those individuals are acutely aware of needs for advancing drug development and applications. For those individuals it is hoped that information presented in this session will generate creative recognition of NASA technologies that might be used to advance drug development and public health.

Once creative recognition is sparked, NASA contacts exist for exploring interests in education, research, development, and partnership. Some of these follow-up contacts are the following.

<http://www.nctn.hq.nasa.gov/index.html> (Technology transfer)  
<http://www.hq.nasa.gov/office/oss/research.htm> (Research opportunities)  
Public Affairs Office (all Space Centers and NASA Headquarters)  
Technology Transfer Office (all Space Centers)  
Equal Opportunity Office (all Space Centers)  
Biotechnology Program (NASA NRA grant mechanism)  
Life Sciences Program (NASA NRA grant mechanism)  
Small Business Programs (SBIR and STTR grant mechanisms)  
Commercial Space Centers (11 total, directed to space flight experimentation)

Most research and development projects begin with experimental feasibility being provided on the ground in standard laboratory environments before space flight experiments are begun. However, interaction with the Commercial Space Centers, for example, can provide an accelerated access to space flight investigations when there is intent to establish a commercial partnership or contract.

## **LAUNCH AND MICROGRAVITY**

Launch has associated with it the excitement of the Fourth of July and the fascination for the great unknown. These ingrained enthusiasms do not eliminate the fact that the experimental concepts of unmatched quiescence, such as is extolled for crystal growth studies, is reached only through a period of turbulent vibration and noise. Neither do they eliminate the fact that the weight and the volume occupied by experimental geometry pose a challenge for achievable experimental design. Additionally, contrary to common assumption, once in orbit the experiment is not significantly outside the Earth's gravitational field, but rather has only achieved escape velocity and is in a state of continual free-fall.

NASA is sophisticated in inventing new descriptive terminology as required. It has nonetheless struggled with finding a good term that combines the

weightlessness experienced in orbital free-fall with the common perception of an absence of gravity. The current term used for this reconciliation is "microgravity". Microgravity is defined as: "a condition of free-fall within a gravitational field in which weight of an object is significantly reduced compared to its weight at rest on Earth".

The concept of the quietude of orbital free-fall has been applied to improved crystal growth (Larry DeLucas; Ewa Ciszak) , smaller and more uniform vesicle formation for microencapsulation (Dennis Morrison), enhanced interactive mammalian cell growth (Bob Richmond; Dennis Morrison), and insights to pharmacologic process (David Bourne). These are subjects that directly impact on drug development and/or application. These are examples of anticipated experimental uses of microgravity and related ground-based experimentation for drug development and/or application.

The need to maximize the efficient use of weight and space within launch vehicles has resulted in miniaturization and simplicity of devices that have then found extended use in biomedical applications. Some of these applications that relate to opportunities of drug development are presented below. These are examples of unanticipated experimental uses of microgravity for drug development and/or application. Maximum attainment of drug development and/or application is realized, however, when the experimental uses of microgravity are anticipated and planned. Anticipation requires first an awareness that this session is intended to provide.

## **NASA TECHNOLOGY EXTENDS TO BIOMEDICAL APPLICATIONS**

### **1. Exobiology**

The finding of fossilized evidence for life in a Martian meteorite is now galvanizing studies by NASA of microbial life in extreme environments on Earth. This new area of discovery will likely lead to new drug discoveries considering that 2/3 of our modern drug inventory is plant- and microbe-related.

## **2. Aerogels**

These are porous, lightweight, potentially transparent, yet strong materials that could be constructed of biocompatible or biodegradable material. Future development with these materials could provide scaffolding for tissue engineering, such as that envisioned for bone or cartilage replacement, with attendant drug support. The extremely porous nature and method of manufacture of these aerogels could also be extended to biodegradable drug delivery systems.

## **3. Virtual Reality**

It is virtually certain that methods of telecommunications will continue to extend outreach of medical care to people in poorly serviced regions. This will include allied health professionals administering care in the field via telecommunication with specialists participating from remote tertiary care facilities. Substantial development of drug application technologies will be needed to support these emerging treatment protocols.

## **4. Physiology In Space**

- a. Unremitting calcium loss from bones in microgravity is a model for osteoporosis. Research on this model would provide opportunity for extending drug leads for the management of this emergent crisis within our aging population.
- b. Orthostatic hypotension that is experienced during space flight is a model for research to develop vasoactive or autonomic drug therapies to combat this refractory condition that is also emergent in our aging population.
- c. Imbalances in circadian rhythm caused by loss of rhythmic light stimulation in space, and the loss of sleep-cycles in space-flight controllers on the ground, provide good opportunities for studies that could provide drug-assisted therapies to improve altered sleep-cycle syndromes, which are again emergent in our aging population.

## **5. High Intensity Light Emitting Diodes**

High intensity LEDs that consume little electrical power, and that are compact, low maintenance, and light weight, have been developed to generate red light to plant biomass growing within the habitat ecosystems required for extended space-flight and off-Earth exploration. These LEDs have been adapted to administer the high intensity red light required for photodynamic therapy (PDT) of solid tumors. The use of LEDs is hoped to overcome the limited use to date of

PDT in cancer therapy that is due largely because of the expense, maintenance, training, and support staff required for the laser systems used until now for this treatment modality. If PDT is thereby extended to use by the private practitioner, then the need to bring improved photosensitizing drugs to market will become acute.

## **NASA TECHNOLOGY APPLIED TO TISSUE CULTURE**

### **1. NASA Bioreactors for tissue-equivalent culture**

#### **a. Principle of operation**

Just as microgravity provides experiments with the quietude of orbital free-fall, the theory for the NASA rotating wall bioreactor provides cells in 3-dimensional culture with continuous free-fall, and thus a low level of dislocation as well as a low level of stress from turbulence or shear. Perhaps the most important aspect for these 3-dimensional cocultures is that this reduction in disturbance allows at least the initial self-assemblies of autologous cell types to colocate with better autocrine and pericrine controls than is found in other tissue culture geometries. The result is often the observation that these initial self-assemblies grow to constructs that have features of tissue-like organization. For such a case, favorable strategies for testing in a given drug development program are immediately obvious.

#### **b. NASA Biotechnology Program**

The concept and development of the NASA bioreactor has been long and involved. Dennis Morrison, one of our presenters, was indeed one of the major contributors to the early conception and design of the bioreactor at the Johnson Space Center in the 1970s. The development and use of the bioreactor has since taken a varied path, but a few years ago was merged with the protein crystal growth interests at the Marshall Space Flight Center to form the NASA Biotechnology Program.

#### **c. NASA/NIH Partnership**

Establishing new biomedical technology within NASA, such as the bioreactor, is hampered in that NASA investigative support is viewed as a blend of specialty and special interest research by the biomedical community. In order to

put NASA bioreactor technology on the biomedical fulcrum a partnership between the NASA Biotechnology Program and the NIH was initiated about 3 years ago. Some results now emergent from that collaboration will be presented by Dennis Morrison in this session.

2. NASA Bioreactors for high-cell density applications

Genetic engineering of eucaryotic cells by use of recombinant DNA technology is now used for the expression of designer drugs and growth factors. The higher the culture density of these engineered cells, then the higher the titer of expressed protein-drug. Three-dimensional tissue culture, such as that supported by the NASA bioreactor, provides this required high density of cells, i.e., about  $10^7$  cells/ml, in a geometry that supports media recovery for subsequent protein-drug extraction.

3. Breast cancer studies in the NASA bioreactor

This topic is separated from the category of tissue-equivalent culture above because breast cancer emphasizes the direction that NASA technologies can be taken to support targeted national priorities of health care. This past December saw NASA commit to the "1997-1999 Women's Outreach Initiative", within which contributions of the space program to advancing health care, nutrition, and medical sciences are stressed. Last October NASA combined with the Congressional Caucus for Women's Issues to present a session "Space Technology Benefits Breast Cancer Research", where topics included 3-dimensional breast cancer research in the NASA bioreactor. Successful applications of new technologies in cancer research invariably involve opportunities for new drug development and/or drug application strategies as well.

Recently, bioreactor studies have been initiated within the NASA Biotechnology Program to provide a breast tissue-equivalent model of heterozygous ataxia-telangiectasia, which is a silent genetic condition predisposing breast cancer susceptibility 5-fold in approximately 1.5 percent of the general population. This susceptibility is thought likely to derive from radiation-induced damage to breast tissue in these susceptible individuals. Initial experiments have shown the induction of self limiting growth for 3-dimensional cocultures of these heterozygous fibroblasts and epithelial cells, for example. Descriptions of the growth of these cells will be presented.